

## **REMARKS**

Claims 37-39 have been amended. No new matter has been added. Claims 36-39 are pending in this application.

### **Rejections under 35 U.S.C. § 112**

#### **Rejections under 35 U.S.C. § 112, 1<sup>st</sup> paragraph**

Claims 36-39 were rejected under 35 U.S.C. § 112, 1<sup>st</sup> paragraph as containing subject matter not described so as to enable one skilled in the art to use the invention. The Examiner asserts that it is unclear what purpose exists for a protein chip in which the reaction product of a reactant ligand and a fusion polypeptide has already been formed.

This rejection under 35 U.S.C. § 112, 1<sup>st</sup> paragraph is respectfully traversed. The specification describes the use of a protein chip as recited in claims 36-39 at least from page 51, line 16 through page 57, line 21; in Figures 3, 6, 7 and 10; in Examples 5-6 (pp. 64-65); and in prophetic Examples 2-3 (pp. 75-77). The term "fusion" as recited in the claims is defined in the specification as "... a molecule comprising a capture polypeptide and a display moiety" (p. 11, lines 10-11). By definition then, the fusion polypeptide recited in the claims includes both the capture polypeptide, which can react specifically with a corresponding reactant ligand, and a display moiety, which is a polypeptide or polynucleotide (p. 11, lines 15-17). It is the display moiety that is the substance of interest, and this display moiety can be used in a variety of applications, including assays, screenings, and catalysis (see p. 17, lines 5-18 and p. 51, lines 17-27). Applicants respectfully submit that the specification contains sufficient description to enable one skilled in the art to use the protein chip recited in claims 36-39 and request that this rejection be withdrawn.

Claims 36-39 also were rejected under 35 U.S.C. § 112, 1<sup>st</sup> paragraph as not enabled for protein chips comprising the surface and moieties recited in claims 37, 38 or 39 "in addition to" the elements recited in claim 36. The Examiner acknowledges that the claims would be enabled if the surface and moieties of claims 37-39 were recited as "further defining" the elements of claim 36.

Applicants respectfully traverse this rejection for the record. Claims 36-39 have been amended to clarify the invention, and these amendments are believed to obviate this rejection under 35 U.S.C. § 112, 1<sup>st</sup> paragraph. Applicants respectfully point out that the specification describes the relationship of a surface and a substrate, for example on page 49, line 2 - page 50, line 7. The surface can be distinct from the substrate, and it is thus proper to describe the surface as being present "in addition to" the substrate. Applicants also point out that claims 37-39 recite that the "-Z" portion of the moieties comprise the reaction product, and thus further define the elements of claim 36. Applicants respectfully submit that the specification contains an enabling description for claims 36-39 and request that this rejection be withdrawn.

#### **Rejections under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph**

Claims 36-39 were rejected under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph as being indefinite. The Examiner asserts that it is unclear if the recitations of claims 37-39 are in addition to the elements of claim 36 or if they further define the elements of claim 36. The rejection of the claims under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph has been obviated by appropriate amendment. As amended, claims 37-39 recite that the substrate comprises a surface and that the plurality of moieties comprising the reaction product (see formula component "-Z") are on at least a portion of this surface. In view of these amendments, Applicants assert that all of the presently presented claims fully meet the requirements of 35 U.S.C. § 112, 2<sup>nd</sup> paragraph and request that this rejection be withdrawn.

#### **Rejections under 35 U.S.C. § 103**

##### **Rejection over Mrksich and Applicants' specification**

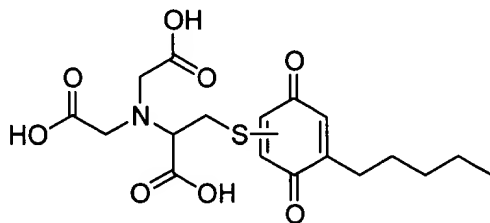
Claims 36-39 were rejected under 35 U.S.C. § 103(a) over Mrksich (Chem. Soc. Rev., 2000, **29**, 267-273) in combination with Applicants' specification at page 15. The Examiner asserts that it would be obvious to substitute the Ni(II) / His-tag combination of Mrksich with a reactant ligand/capture polypeptide pair such as cutinase / nitrophenylphosphonate. In making this assertion, the Examiner has pointed to Table A on page 15 of the specification, which includes both a cutinase / nitrophenylphosphonate system and a quinone-NTA / His-tag polypeptide system.

The rejection of the claims over Mrksich and Applicants' specification is respectfully traversed. Applicants respectfully point out that a *prima facie* case of obviousness has not been established. The Examiner has not provided a motivation or suggestion to combine the biosensors disclosed in Mrksich with a reactant ligand/capture polypeptide pair such as cutinase / nitrophenylphosphonate. Rather, the Examiner has asserted that such a combination is simply a substitution of a known equivalent. As noted in the MPEP, however:

In order to rely on equivalence as a rationale supporting an obviousness rejection, **the equivalency** must be recognized in the prior art, and **cannot be based on applicant's disclosure or the mere fact** that the components at issue are functional or mechanical equivalents. [MPEP § 2144.06, emphasis added]

Thus, the mere inclusion of two reactant ligand/capture polypeptide systems in a list within Applicants' specification is insufficient to establish obviousness based on equivalence.

Moreover, Applicants point out that the quinone-NTA / His-tag polypeptide system listed in Table A is not equivalent to the Ni(II) / His-tag polypeptide system disclosed in Mrksich. The quinone-NTA / His-tag system is described on page 33, line 16 – p. 34, line 4 and in Examples 12-13 (pp. 72-75). This system involves a compound containing a conjugate of nitrolotriactic acid (NTA) and a substituted quinone:



The covalent binding of this conjugate with a modified His-tag moiety is contrasted in the specification with the non-covalent, relatively weak binding of Ni(II) complexes with histidine residues. The disadvantages of conventional Ni(II) / His-tag systems as described in Mrksich are also noted in the background of Applicants' specification (p. 2, lines 8-18). Thus, the reactant ligand/capture polypeptide systems that involve covalent binding, such as quinone-NTA / His-tag and cutinase / nitrophenylphosphonate, are not equivalent substitutions for Ni(II) / His-tag.

With respect to the Examiner's note that claims 36-39 are not limited to the use of any particular ligand/fusion polypeptide combination, Applicants point out that, in accordance with the Patent Office's guidelines, the terms "reactant ligand", "fusion polypeptide" and "capture polypeptide" are to be given their broadest reasonable interpretation in light of any clear definitions provided in the specification (MPEP § 2111 – 2111.01). These terms are defined on pages 10-11 of Applicants' specification.

Claims 36-39 are not obvious over Mrksich in combination with Applicants' specification. No suggestion or motivation to combine Applicants' specification with the biosensors of Mrksich has been set forth, nor has a valid equivalence been established between the systems described by Applicants and the systems disclosed in Mrksich. Accordingly, a *prima facie* case of obviousness has not been presented, and Applicants request that this rejection be withdrawn.

#### **Rejection over Yousaf et al. and Applicants' specification**

Claims 36-39 were rejected under 35 U.S.C. § 103(a) over Yousaf et al. (J. Am. Chem. Soc., **1999**, 121, 4286-4287) in combination with Applicants' specification at page 15. The Examiner asserts that it would be obvious to combine the self-assembled monolayers (SAM's) of Yousaf et al. with a reactant ligand/capture polypeptide pair such as cutinase / nitrophenylphosphonate. In making this assertion, the Examiner again points to Table A on page 15 of the specification, as noted in the rejection involving Mrksich. The Examiner has cited the Yousaf et al. reference only with respect to its disclosure of peptide ligands attached to gold through an alkanethiolate-polyethylene glycol linkage.

The rejection of the claims over Yousaf et al. and Applicants' specification is respectfully traversed. Applicants respectfully point out that a *prima facie* case of obviousness has not been established. The Examiner has not provided any motivation or suggestion to combine the SAM's disclosed in Yousaf et al. with a reactant ligand/capture polypeptide pair such as cutinase / nitrophenylphosphonate. Moreover, unlike the above rejection involving Mrksich, the Examiner has not asserted that any of the reactant ligand / capture polypeptide pairs listed in Applicants' specification are equivalent to a system disclosed in Yousaf et al.. Applicants note that the first

paragraph of the reference does mention the Ni(II) / His-tag system; however, this disclosure serves to teach away from the systems described by Applicants, as the reference points out the poor long-term stability of Ni(II) / His-tag. As noted above, the Ni(II) / His-tag system is not equivalent either to the quinone-NTA / His-tag system or to the cutinase / nitrophenyl-phosphonate system.

Claims 36-39 are not obvious over Yousaf et al. in combination with Applicants' specification. No suggestion or motivation to combine Applicants' specification with the biosensors of Yousaf et al. has been set forth, nor has a valid equivalence been established between the systems described by Applicants and the systems disclosed in Yousaf et al. Accordingly, a *prima facie* case of obviousness has not been presented, and Applicants request that this rejection be withdrawn.

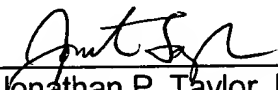
### Conclusion

In conclusion, all of the grounds raised in the outstanding Office Action for rejecting the application are believed to be overcome or rendered moot based on the amendments and remarks above. Thus, it is respectfully submitted that all of the presently presented claims are in condition for allowance. Should the Examiner feel a discussion would expedite the prosecution of this application, the Examiner is kindly invited to contact the undersigned.

Also submitted at this time is a Petition For Extension Of Time for two (2) months.

Respectfully submitted,

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